THE ETIOLOGY OF PORAL CLOSURE

An Experimental Study of Miliaria Rubra, Bullous Impetigo and Related Diseases of the Skin*

I. An Historical Review of the Causation of Miliaria

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INTRODUCTION

In this paper I describe some of my further work on the minute pathologic reactions which occur in the tropics in primary relationship to the pores of the skin. Although most of the observations concern the sweat pores and miliaria rubra ("prickly heat") some of the conclusions may also apply to the pilosebaceous follicles. Secondary and incidental involvement of pores by diffuse diseases of the skin such as atopic dermatitis (1) is not especially considered. As a matter of convenience, the terms "pore" and "poral" will be used here as referring to the sweat pores and the term "miliaria" will denote miliaria rubra.

In an earlier account (2), of which this is an elaboration, I described how the last convolution or two of the sweat duct has walls composed of a laminated ring-like or tube-like condensation of keratin called the keratin ring of the pore (see Plates 1 and 2). I suggested that the prime and essential lesion of miliaria is a subtle closure of this keratin ring and that, as a direct result of this change, clinical miliaria ensues. A case was also made out for the belief that a lipoid depletion of the stratum corneum (and its keratin rings) is the factor which closes the pores in miliaria.

More recent experience has modified these opinions. Whereas the keratin ring has gained even added significance, it now appears that lipoid depletion is only one of a number of factors capable of producing closure. Among the new factors to be incriminated are simple covering (envelopment) of the skin, too much soaping and the application of lipoid solvents to the skin. Of still greater import is the evidence, also given here, which suggests that primary staphylococcal infection is the usual or predominating cause of miliaria rubra under ordinary conditions.

Poral closure appears to be a prevalent or "type" reaction of the skin even in cooler climates. It is apt to masquerade under a large number of facile, incomplete or incorrect diagnoses such as "heat rash," "sweat rash," "infantile rash," "occupational (e.g. miners' (3)) rash," "maculo-papular rash," "pyoderma" and "contact dermatitis." Shelley, Horvath, Weidman and Pillsbury (4) have recently found that certain noxae (iontophoresis, application of heat or cold,

* These studies were begun and largely carried out in the islands of the South-West Pacific whilst the author served as a pathologist in the Australian army. They are based on some 15,000 serial histologic sections.

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ultra-violet light, wet dressings, various chemicals including aluminium chloride) produce poral closure (sweat retention anhidrosis (1)). At least one form of impetigo, tropical bullous impetigo (5),* is an obstructive poral disease and it is likely that other forms, notably impetigo ("pemphigus") neonatorum (6) are also. The ill-defined conditions referred to by Davies, Dixon and Stuart-Harris (7) as "impetiginized seborrhoea" may well represent yet another group of poral lesions.

Occupying the unexplored borderland between health and frank disease, miliaria-like conditions are probably the most frequent of all cutaneous aberrations. Although often scorned as trivial, they merit special consideration as warnings of later and more manifest disorder. Furthermore, although tedious to study, they offer the means, perhaps the only means, whereby we may hope

PLATE 1. The lamellated keratin ring of a normal sweat pore in cross section. (Haematoxylin and Biebrich Scarlet. × 900.)

to unravel a web of causation which becomes hopelessly confused in many chronic dermatoses.

Another good reason for emphasizing poral closure derives from its evil effect on the tolerance of man to hot atmospheres (8).

To summarize, this series of papers embodies two chief concepts. They are firstly that miliaria is the prototype of an exceedingly common cutaneous reaction and secondly that it is the clinical manifestation of a fundamental and more subtle lesion, namely poral closure.

HISTORICAL REVIEW

Every aspect of miliaria has been debated, but especially its pathology and etiology. Although much could therefore be written concerning past studies, a

* In a personal communication, Sulzberger informs me that in a few unpublished studies carried out on Guam, Zimmerman and he were unable to demonstrate a connection between the blebs and pustules of tropical bullous impetigo and the sweat or apocrine pores. He states however that the material studied was too scant to permit conclusions.

complete review would be unprofitable, since many accounts are based on little or no objective evidence. Fundamentally opposing views have been advanced as to the pathology.

PLATE 2. A longitudinal section of a terminal sweat duct, the actual opening of the pore being just outside the plane of the section. The last portion of the duct is lined by keratin which appears almost black. In the deeper duct a refractile internal cuticle may be detected. A continuous investment of granular cells is prominent. (H. and B. S. × 1800.)

They mainly concern:

1. Whether or not the sweat glands implicated by miliaria are obstructed. For instance, some have held that affected skin is hyperhidrotic rather than anhidrotic.
2. Whether or not the sweat ducts communicate with the miliarial vesicles.

These two disputed points were discussed in detail in the earlier paper (2) written in 1944. It was then suggested that since closure of the keratin ring is

the initial lesion of miliaria, every affected sweat gland is obstructed from the start of the clinical disease. Furthermore, the sweat ducts do as a rule communicate with the vesicles. Sweat escapes into the cutaneous tissue spaces either directly (2) or, according to Sulzberger and Zimmerman (9) by rupture of ducts, by transudation through duct walls or by an absorptive process. These writers in their independent studies demonstrated the fundamental point that miliaria s associated with poral closure (anhidrosis).

To turn to the pioneers in this field, Robinson (10) seems to have been the first to record a study of miliaria. Although his paper, published in 1884, is unobtainable in Australia, it appears from Stelwagon (11) that he was the first to recognize that miliaria is a disease of the sweat glands. His knowledge of two important aspects of its pathology is indicated by his reference (11) to "retention" and to "transudation" of sweat. Apparently he had no definitive ideas on etiology, as he is quoted as merely stating that the process is inflammatory.

Pollitzer (12), publishing in 1893, was the first to study miliaria in detail, his conclusions being based on the examination of serial sections from eight cases. Unlike many of those who came later, he had no doubt that miliaria involves obstruction of the sweat glands. However, he was perhaps inclined to put excessive emphasis on duct dilatation as opposed to duct rupture and the associated escape of sweat into the tissues. Yet his ideas on etiology are still precise and illuminating. Being unsatisfied to incriminate "oversweating", alcoholic drinks and other dubious or remote causes, he held that

> "the condition is evidently due to imbibition (of the stratum corneum)with water, with sweat. An epidermis which is bathed in perspiration, retained as it commonly is by wet underclothing, cannot cornify*; and in imbibing water, the cells swell and swell, of course, in all directions, laterally as well as vertically. Cells which are well impregnated with fat cannot imbibe water and therefore will not swell up and occlude the sweat ducts when soaked with perspiration."

Pollitzer then instances the freedom of the well-oiled Negro from miliaria and the toll of the disease among Englishmen in India who take "a couple of tubs a day". Pollitzer did not give any experimental support for his opinions and they may have been based simply on clinical acumen. Nevertheless, the fat-deficiency part of his concept is partially supported by the observations described in my earlier paper (2).

Unna (13), writing in 1896, agreed with Pollitzer that the sweat pores are closed in miliaria, but disagreed as to the cause. In particular, he disputed that swelling of the stratum corneum causes the blockage and he instanced the rather indecisive and unproven point that washer-women do not suffer in that way. Unna was disposed to think that miliaria is an inflammatory and infective disorder, but he did not specify the infecting agent. He said that "the examination of the sweat pores in prickly heat for bacteria is of great importance", a statement which remains as true today as when he made it. As a matter of interest, Unna and Török introduced the concept that the non-inflammatory state called crystallina (sudamen or miliaria crystallina) is histologically analogous to miliaria rubra, differing only in that the obstruction and thus the vesicles are more superficial. However Unna was careful to point out that crystallina and miliaria are otherwise quite distinct.

Acton (14) wrote in 1926: "There are others who believe that with the excessive perspiration that occurs in this (humid) season, there is not enough oily secretion to protect the sweat gland mouths; hence, these become damp and sodden and then liable to *secondary* infection."

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* In this place, Pollitzer seems to refer obliquely to parakeratotic (keratin) plugs in the pores (2). Such plugs, as distinct from keratin rings which are merely closed, do not appear to be present from the beginning of individual miliarial lesions, but follow later (2). Yet, Pollitizer's ideas as to imbibition seem equally applicable, at least in a theoretical sense, to the otherwise normal keratin rings of the pores.

Acton's personal belief was that miliaria is due to a *primary* infection of the sweat gland mouths by *Staphylococcus aureus* and *Staphylococcus albus* and, further, he believed that the wearing of clothes and the over-use of soap are contributory. He also noted the frequent association of a staphylococcal folliculitis. Although Acton gives no experimental data of his own, his opinion as to infection also receives support in the work soon to be described. However, not all would agree with his assertion, shared by Andrews (15) that seborrhoea is predisposing. Sulzberger and Emik (16) do no mention seborrhoea in their clinical study, and as already noted, others have stressed a sebaceous deficiency.

Smith's experimental work, published in 1927 (17), has often been accepted. By means of a lint pad and adhesive tape, Smith applied a culture of a monilia (candida (18)) to the skin of normal volunteers. He believed that true miliaria resulted in an unspecified number of instances.

Smith was probably not justified in incriminating his extraneous monilia to the complete exclusion of the other micro-organisms already resident on the skin of his subjects. The skin harbours a prolific flora (19) at a density of at least 10,000 bacteria per square cm. of surface (20). Pathogens such as *Staphylococcus aureus* (21, 22) are often present.

On the description he gives, it is difficult to be sure that Smith produced true miliaria. Moreover he seems to have confused his monilia with a saprophyte (*Pityrosporum ovale* of Malassez (23, 24)) which is commonly found in the follicles of normal skin. That he dealt in part with a monilia seems clear from the ease with which he could grow the organism *in vitro*; his Figure 9 also suggests a monilia. On the other hand, his Figures 1, 25, 26 and 27 strongly suggest the *Pityrosporum*.

In a recent summary, Napier (25) states that most workers now question the role of monilia in miliaria. Whilst this is true, Napier is not necessarily correct when he asserts that Smith reproduced moniliasis and not miliaria. Quite apart from the effect, if any, of his monilial culture, Smith may actually have induced a miliaria-like condition for no other reason than that he kept a patch of skin closely covered during the course of his experiments. For it will be shown in Part II that the simple procedure of covering the skin often induces a state of poral closure.

To turn to more recent accounts, Sulzberger and coworkers(1), and particularly Shelley, Horvath, Weidman and Pillsbury (4) have carried out important experimental studies on poral closure (sweat retention anhidrosis (1)). They inflicted various physical and chemical injuries on the skin and demonstrated ensuing poral closures and clinical lesions when the subjects were made to sweat. In their first paper Shelley and collaborators (4) dealt chiefly with the effect of iontophoresis on the pores. By the use of this agent they were able to bring about a state of anhidrosis and associated crystallina* (miliaria crystallina or sudamen). As they did not regularly elicit the inflammation, deep obstruction or the large parakeratotic plugs which are such characteristic features of true miliaria rubra, it is difficult to know how far their results apply to the more serious disease. Further, what may be true of crystallina is not necessarily true of miliaria. Although related in their lesions, the two diseases do not seem to have the same cause (Unna (13)).

An important if not decisive element in the experiments of Shelley *et al.* was that some form of diffuse damage of considerable severity was inflicted on the

* Unna (13) preferred the simple term "crystallina" to "miliaria crystallina" and his usage will be followed here so as to avoid any confusion with miliaria rubra.

superficial interfaces of the skin such that portion of the stratum corneum was shed some three weeks later. It is thus possible that the occlusive effect on the pores was incidental to a more general change in the stratum corneum. In other words, the abnormalities they observed in sweating may have been simply due to the fact that a continuous sheet of the stratum corneum had been loosened as the result of injury. During my studies in the tropics, crystalline vesicles exactly like those they show in their Photograph No. 2 were sometimes noted a few days following erythematous sunburn and also after the application of salicylic acid and of mercuric chloride to the skin.

Intimately bound up with this matter of crystallina is the question whether it is the rule for the sweat pores to close in some impermanent fashion during periods of glandular rest. Most persons are familiar with a miliaria-like prickling in the skin just prior to an outpouring of sweat when unaccustomed exercise is taken in wintertime; the pruritus in such circumstances is most likely due to a temporary distension of the ducts (and thus, excitation of sensory nerves) consequent on some initial poral resistance which is normally soon overcome by the mounting pressure of secretion. On the basis of such poral closure during rest it is not difficult to explain the occurrence of crystalline vesiculation providing a superficial part of the stratum corneum is not normally adherent.

The exact nature of this apparent poral resistance arising during rest is unknown. Perhaps it is due to dried secretion but more likely it is due to a concertina-like approximation or valve-like collapse of the final coils of the keratin ring. Photograph 6 of Shelley *et al.* (4) might fit in with this simple explanation. On the other hand, it seems clear that in true miliaria rubra (2, 9) the blockage of the pores is of a far more drastic and permanent character.

Approaching miliaria from a systemic rather than a local angle, Horne and Mole (26) have recently suggested that miliaria is caused by a disturbance of the salt and water balance of the body. They base their suggestion on observations which indicate to them that increased sodium chloride intake and decreased water intake aggravate prickly heat and that the opposite treatment relieves the disease.

As a statistical study, Horne and Mole's work is open to criticism in that their cases were few and all variables were not controlled or were beyond control. Moreover these observers apparently took notice of the intensity of a symptom (prickling) as a valid index of the severity of disease; they used an arbitrary grading, based partly on the prickling and partly on the rash (miliaria). Although this procedure can be justified clinically there is some doubt about its merit in a statistical sense. Bias, at least on the part of the subjects, could have colored the results; for it seems that the subjects were aware of their treatment and even of the effect expected of it. Stricter precautions, such as the use of a control group on *dummy* salt tablets, appear to have been necessary.

Further work should therefore be done before salt and water imbalance can be accepted as a primary causative factor. In the meantime, it is necessary to remember that the anhidrosis associated with miliaria itself leads to an alteration of salt and water balance (8).

SUMMARY OF PART I

Until recent times the causation of miliaria rubra has been more debated than investigated. Past workers have variously blamed lipoid depletion of the skin, edema of the stratum corneum and poral infection either separately or in combination. As regards infection there has been a further difference of opinion as to whether it is primary or secondary.

Smith's (17) work has been generally accepted over the past twenty years but there are good reasons for doubting his yeast-like organism as the cause of miliaria. Others have blamed staphylococcal infection but no experimental support for their views has been available.

More recently (2) some definite evidence has been brought forward in regard to a positive role of lipoid depletion, this aspect being further discussed in the present papers on poral occlusion.

The application of various artificial injuries by Shelley *et al.* (4) sheds light on crystallina and on the reactions of the stratum corneum and its keratin rings. However it is uncertain at the moment just how far this new knowledge should be applied to miliaria rubra as usually encountered.

The belief of Horne and Mole that disturbed salt and water metabolism may cause or contribute towards miliaria requires further investigation.

(The References will be given at the end of Part IV.)